REMARKS

Claims 31, 36-38, 40-47, and 55 are pending in this application for the Examiner's review and consideration.

The specification was amended to correct several typographical errors. The paragraph beginning at page 8, line 1 was amended to correct the name of compound VIB 106 in the title of Example 2 to 1-[4-Methyl-7-(2-methylprop-1-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)-propen-1-one. That there was a typographical error in the name of the compound is evident from the structural formula on page 18 of the specification that clearly shows that structure VIB 106 is 1-[4-Methyl-7-(2-methylprop-1-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)-propen-1-one and not 1-[4-Methyl-7-(3-methylbut-2-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)-propen-1-one. The paragraph beginning at page 16, line 21 was amended to replace the term "ml" with "µl". A person of skill in the art would readily recognize that this is a typographical error since the capacity of each well of a 96 well plate is only about 200 µl.

Claim 31 was amended to add the proviso that when R^1 is CH_3 and R is OH, then Ar cannot be 3-pyridyl or 4-pyridyl; and when R^1 is CH_3 and Ar is 3-pyridyl, then R cannot be $OCH_2CH=CH_2$ or $OCH_2C(CH_3)=CH_2$. Claim 36 was amended to replace the term "$N(R^8)(R^8)$" with "$N(R^6)(R^8)$." (*See e.g.*, Specification, page 3, line 20). Claim 40 was amended to replace the term "R" with "R^{10}". (*See e.g.*, Specification, page 3, line 23). Claim 43 was amended to add that R is selected from $OCH=C(CH_3)_2$, $OCH_2CH=C(CH_3)_2$, $OCH_2C(CH_3)=CH_2$, $OCH_2CH=CH_2$, and $OCH_2C\equiv CH$ in addition to OH. (*See e.g.*, Specification, page 5, lines 14-15, and representative compounds depicted on pages 18-20). Claim 47 was amended to correct the name of the compound to 1-[4-methyl-7-(2-methylprop-1-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one. (*See e.g.*, Specification, page 18, structure VIB 106).

No new matter has been added. For the reasons that follow, it is believed that the claims are in condition for allowance.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 36, 40, and 43 were rejected under 35 U.S.C. § 112, second paragraph, for the reasons set forth on page 3 of the Office Action. Specifically, the Examiner alleged the following:

1. Claim 36 should read $N(R^6)(R^8)$;
2. Claim 40 should read R^{10};
3. In claim 43, OCH_2R^1 does not have an antecedent basis; and

4. In claim 43, R_1 should read R^1.

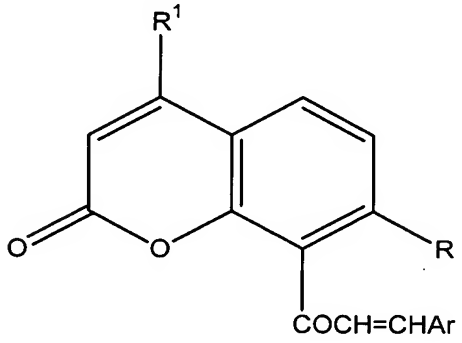
Claims 36, 40, and 43 have been amended according to the Examiner's suggestions. For the above reasons, Applicants respectfully request that the rejection of claims 36, 40 and 43 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

THE REJECTION UNDER 35 U.S.C. § 102(B) SHOULD BE WITHDRAWN

Claims 31, 36, 40, 43-46, and 55 were rejected under 35 U.S.C. § 102(b) as being anticipated by Chemical Abstracts (CA) 92:58620 (FR Patent No. 2,378,956) and CA 95:203793 (J. Indian Chem. Soc. (1981), 58(9), 880-882) for the reasons set forth on page 2 of the Office Action. Applicants respectfully traverse the rejection.

As the Examiner is aware, a prior art reference must disclose all the limitations of a claim in order to anticipate the invention recited by that claim. MPEP § 2131. There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). Put another way, "[a] claim is anticipated and therefore invalid only when a single prior art reference discloses *each and every limitation of the claim*". *Glaxo Inc. v. Novapharm Ltd.* , 52 F.3d 1043, 1047, *cert. denied*, 116 S. Ct. 516 (1995) (citations omitted) (emphasis added).

The claimed invention is directed, in part, to certain novel chalcones, chalcone derivatives and chalcone analogues. (*See e.g.*, Specification, page 2, lines 4-5). As amended, independent claim 31 recites a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl which may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO_2, (f) CF_3, (g) C_{1-4} alkyl, (h) SCH_3, (i) $NHCOCH_3$, (j) $N(R^6)(R^8)$ wherein R^6 and R^8 are the same or

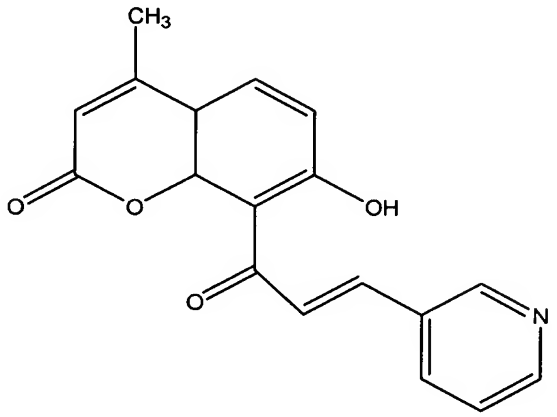
different and each represents H or C_{1-4} alkyl, (k) OR^{10} wherein R^{10} represents a saturated or unsaturated C_{1-6} straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO_2 and CF_3, and (l) - $OCOR^{11}$ wherein R^{11} represents a saturated or unsaturated C_{1-6} straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR^{10} or $OCOR^{11}$ wherein R^{10} and R^{11} are as defined above; and R^1 represents H or a C_{1-6} straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO_2 and CF_3;

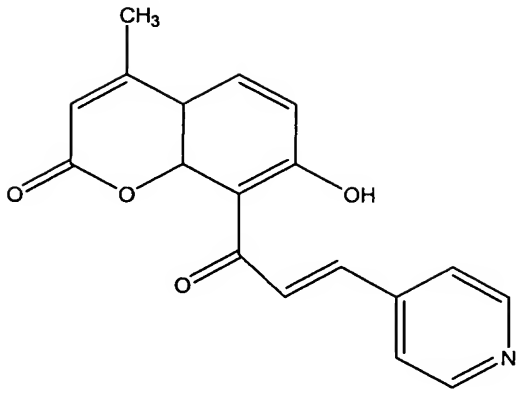
with the proviso that when R^1 is CH_3 and R is OH, then Ar cannot be 3-pyridyl or 4-pyridyl; and

when R^1 is CH_3 and Ar is 3-pyridyl, then R cannot be $OCH_2CH=CH_2$ or $OCH_2C(CH_3)=CH_2$.

CA 95:203793 discloses various γ-pyrano-coumarins synthesized from *o*-hydroxy-acetyl-coumarins, including a compound with the following structure:



CA 92:58620 discloses γ-pyrano-coumarins, including a compound with the structure:



Claim 31, as amended, does not encompass the compounds disclosed in CA 95:203793 and CA 92:58620. Specifically, the proviso of claim 31, as amended, excludes the compounds disclosed in CA 95:203793 and CA 92:58620. Thus, amended claim 31, and its dependent claims 36, 40, 43-46, and 55 are not anticipated by CA 95:203793 or CA 92:58620. For the above reasons, Applicants respectfully request that the rejection of claims 31, 36, 40, 43-46, and 55 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103(A) SHOULD BE WITHDRAWN

Claims 31, 36, 40, 43-46, and 55 were rejected under 35 U.S.C. § 103(a) as being obvious over Chemical Abstracts (CA) 92:58620 (FR Patent No. 2,378,956) and CA 95:203793 (J. Indian Chem. Soc. (1981), 58(9), 880-882) for the reasons set forth on page 2-3 of the Office Action. More specifically, the Examiner alleged that isomers and/or homologs of known compounds are suggested for the art uses. Applicants respectfully traverse the rejection.

As the Examiner is well aware, three basic criteria must be met to establish a case of *prima facie* obviousness: first, there must have been at the time of the invention a motivation to combine the references cited or modify the existing reference; second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious; and third, there must have been at the time of the invention a reasonable expectation of success. MPEP § 2142.

As noted above, the compounds disclosed in CA 95:203793 and CA 92:58620 are not encompassed by claim 31, as amended. As discussed above, there is no disclosure or suggestion in CA 95:203793 or CA 92:58620, either individually or in combination, of the compounds recited in claim 31.

Furthermore, contrary to the Examiner's allegations, the compounds recited in claim 31 are not homologs or isomers of the compounds disclosed in CA 95:203793 or CA

92:58620. Homologs are compounds differing regularly by the successive addition of the same chemical group, *e.g.*, by $-CH_2$ groups. (*See e.g.*, Manual of Patent Examining Procedure [MPEP] § 2144.09). Isomers are molecules having the same number and kind of atoms and hence the same molecular weight, but differing in respect to the arrangement or configuration of the atoms. (*See e.g.*, Hawley's Condensed Chemical Dictionary, Twelfth Edition, page 656). Applicants submit that based on these definitions, the compounds in claim 31 cannot be considered homologs or isomers of the compounds disclosed in CA 95:203793 or CA 92:58620, since the clamed compounds do not differ from the compounds disclosed in CA 95:203793 or CA 92:58620 by the successive addition of a same chemical group or by the arrangement of atoms. Rather, the claimed compounds have *different* functional groups from those disclosed in CA 95:203793 or CA 92:58620. Thus, neither CA 95:203793 nor CA 92:58620 renders claims 31, 36, 40, 43-46, and 55 obvious. For the above reasons, Applicants respectfully request that the rejection of claims 31, 36, 40, 43-46, and 55 under 35 U.S.C. § 103(a) be reversed and withdrawn.

CONCLUSION

Applicants believe the application is in condition for allowance and request reconsideration of the claims and allowance thereof. If the Examiner has any questions or suggestions to expedite allowance of this application, however, the Examiner is respectfully invited to call the undersigned to discuss the matter further.

A Petition for Extension of Time, with provision for the required fee, to extend the time for responding by one (1) month from October 30, 2003 to and including December 1, 2003, since November 30, 2003 falls on a Sunday, is also attached hereto.

No fee is believed to be due for this submission. Should any fee be required, however, please charge such fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: December 1, 2003

Paul E. Dietze (Reg. No. 45,627)

For: Thomas G. Rowan (Reg. No. 34,419)

PENNIE & EDMONDS LLP
1667 K Street, N.W.
Washington DC 20006

Hawley's

Condensed Chemical

Dictionary

TWELFTH EDITION

Revised by

Richard J. Lewis, Sr.

VAN NOSTRAND REINHOLD COMPANY
New York

isoeugenol acetate. See acetylisoeugenol.

isoeugenol ethyl ether. (1-ethoxy-2-methoxy-4-propenyl-benzene). $C_3H_5(CH_3O)C_6H_3OC_2H_5$.
Properties: Synthetic, white, crystalline powder; mp 64C; insoluble in water; soluble in alcohol, ether, benzene. Combustible.
Use: Sweetening agent and odorant fixative.

isoflurophate. See diisopropyl fluorophosphate.

"Isoforming." Proprietary process for fixed-bed hydroisomerization, requiring a non-noble-metal catalyst. Claimed to give high yields of C_8 (xylene) isomers with low hydrogen consumption and minimal catalyst regeneration.

isoheptane. See 2-methylhexane.

isohexane. CAS: 107-83-5. C_6H_{14}. A mixture of branched-chain isomers.
Properties: Colorless liquid, boiling range 54-61C, d 0.671 (15.5/15.5C), flash p −26F (−32C) (CC).
Grade: Commercial.
Hazard: Highly flammable, dangerous fire and explosion risk, explosive limits in air 1-7%.
Use: Solvent, freezing-point depressant.

isolan. See 1-isopropyl-3-methyl-5-pyrazolyl-dimethylcarbamate.

isolated double bond. Double bond separated by more than one single-bond linkage from the next double bond.

isolation. Identification and separation of a pure substance which is present in trace amounts in a complex mixture. A famous instance of this was the isolation of polonium (1898) and radium (1912) from pitchblende by the Curies by coprecipitation techniques followed by repeated fractional crystallization.

isoleucine. (2-amino-3-methylpentanoic acid; Ile). CAS: 73-32-5.
$CH_3CH_2CH(CH_3)CH(NH_2)COOH$. An essential amino acid, found naturally in the L(+) form.
Properties: Crystals, slightly soluble in water, nearly insoluble in alcohol, insoluble in ether.
Derivation: Hydrolysis of protein (zein, edestin), amination of α-bromo-β-methylvaleric acid.
Use: Medicine, nutrition, biochemical research.

"Isomate" [*Upjohn*]. TM for isocyanate foam systems. Available as non-burning, pour-in-place froth, or spray foams.

isomer. (1) One of two or more molecules having the same number and kind of atoms and hence the same molecular weight, but differing in respect to the arrangement or configuration of the atoms. Butanol (C_4H_9OH or $C_4H_{10}O$) and ethyl ether ($C_2H_5OC_2H_5$ or $C_4H_{10}O$) have the same empirical formulas but are entirely different kinds of substances; normal butanol ($CH_3CH_2CH_2CH_2OH$) and isobutanol ($[CH_3]_2CHCH_2OH$) are the same kinds of substances, differing chiefly in the shape of the molecules; sec-butanol ($CH_3CH_2OCH_2CH_3$) exists in two forms, one a mirror image of the other (enantiomer). Isomers often result from location of an atom or group of a compound at various positions on a benzene ring, e.g., xylene, dichlorobenzene. (2) Nuclides, (i.e., kinds of atomic nuclei) having the same atomic and mass numbers, but existing in different energy states. One is always unstable with respect to the other, or both may be unstable with respect to a third. In the latter instance the energy of transformation in the two cases will differ.
See also geometric isomer, optical isomer.

isomerization. A method used in petroleum refining to convert straight-chain to branched-chain hydrocarbons or alicyclic to aromatic hydrocarbons, to increase their suitability for high-octane motor fuels. For example, butane (a gaseous paraffin hydrocarbon, $CH_3CH_2CH_2CH_3$) can be slightly modified in structure by catalytic reactions to give the isomeric isobutane ($CH_3CH_3CHCH_3$), used as a component of aviation fuel. Similarly, methylcyclopentane can be isomerized to cyclohexane, which is then dehydrogenated to benzene. Isomerization techniques were introduced on a large scale during World War II.
See also isomer, chain.

α-isomethylionone. (γ-methylionone). $C_{14}H_{22}O$.
Properties: Slightly yellow liquid, d 0.925-0.929 (25/25C), refr index 1.5000-1.5010 (20C), flash p 217F (102.7C) (TCC), soluble in 5 parts of 70% alcohol. A synthetic product. Combustible.
Use: Floral perfumes, particularly of a violet character; flavoring.

isomorphism. The state in which two or more compounds that form crystals of similar shape have similar chemical properties and can usually be represented by analogous formulas, e.g., Ag_2S and Cu_2S.

is nipecaine hydrochl ride. See meperidine hydrochoride.

isonitrile. See carbylamine.